

# WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention

## Use of human papillomavirus (HPV) DNA genotyping

Web Annex B.  
Evidence-to-decision tables



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This publication forms part of the WHO document entitled *WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention: use of human papillomavirus (HPV) DNA genotyping*. It is being made publicly available for transparency purposes and information, in accordance with the *WHO handbook for guideline development*, 2nd edition (2014).

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The additional web annex for this guideline is:  
Web Annex A. Evidence summaries. Available at: <https://doi.org/10.2471/B09736>

## Evidence-to-decision table

### Population, intervention, comparators and outcomes

Should World Health Organization (WHO) recommend the use of human papillomavirus (HPV) DNA extended or limited genotyping over other HPV DNA testing to screen women in the general population to prevent cervical cancer?	
Population	Women in the general population
Intervention	HPV DNA extended or limited genotyping to screen women to prevent cervical cancer, followed by ablative treatment for those eligible
Comparison	No genotyping
Main outcomes	<ul style="list-style-type: none"> <li>•Cervical cancer</li> <li>•Mortality</li> <li>•Pre-cancer treatments and adverse events</li> </ul>
Setting	Outpatient
Perspective	Population
Background	<p><b>HPV DNA tests</b> are available with no genotyping, limited genotyping or extended genotyping offering different screening and management strategies to prevent cervical cancer screening.</p> <p>Results from HPV DNA tests can be categorised into four groups based on relative attributable fraction in cervical cancer (informed by the International Agency for Research on Cancer (IARC) Monograph No. 90, the IARC Handbook volume 18, Wei et al. 2024<sup>1,2,3</sup> and WHO target product profiles (TPPs) for HPV screening tests):</p> <p>Group 1a contains HPV16            Group 1b contains HPV18/45            Group 1c contains HPV31, 33, 35, 52 and 58            Group 1d contains HPV39, 51, 56 and 59</p>
Conflict of interests	None

<sup>1</sup> Human papillomaviruses. IARC monographs on the evaluation of carcinogenic risks to humans, Vol. 90. Lyon: International Agency for Research on Cancer; 2007 (<https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Human-Papillomaviruses-2007>).

<sup>2</sup> International Agency for Research on Cancer. IARC handbooks of cancer prevention: cervical cancer screening, Vol. 18. Lyon: IARC Press; 2022 (<https://publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Cervical-Cancer-Screening-2022>).

<sup>3</sup> Wei F, Georges D, Man I, Baussano I, Clifford GM. Causal attribution of human papillomavirus genotypes to invasive cervical cancer worldwide: a systematic analysis of the global literature. *Lancet*. 2024;404(10451):435–44. ([https://doi.org/10.1016/S0140-6736\(24\)01097-3](https://doi.org/10.1016/S0140-6736(24)01097-3)).

## Assessment

Desirable effects																															
How substantial are the desirable anticipated effects?																															
Judgement	Research evidence																														
<ul style="list-style-type: none"> <li>○ Trivial</li> <li>○ Small</li> <li>○ Moderate</li> <li>○ Large</li> <li>● <b>Varies</b></li> <li>○ Don't know</li> </ul>	<p>Two methods were used to determine the effects of different HPV DNA testing to screen women in the general population to prevent cervical cancer: 1) An analysis from multiple data sets of the risk of cervical cancer lesions (cervical intraepithelial neoplasia [CIN]3+) given type of HPV DNA; and 2) Modelling of the effects of different HPV DNA testing (including triage or no triage and treatment).</p> <p><b>Risk of CIN3+ based on HPV DNA type</b></p> <p>A systematic review of published and unpublished data from cross-sectional and longitudinal studies with a pooled meta-analysis of the cumulative risks of CIN2+, CIN3+ and cervical cancer associated with ranked series of HPV types and groups of types and by follow-up time were conducted. The Guideline Development Group (GDG) agreed to rank HPV types according to the WHO TPP groups and agreed using cumulative CIN3+ or cancer over time as a proxy of disease detection.</p> <p>The cumulative incidence of CIN3+ by infection with a given HPV type at baseline is shown in the figure below. Curves are scanned, digitized and translated into a dataset using Digitzelt. Adapted from Demarco, 2020<sup>4</sup>.</p> <div style="text-align: center;"> </div> <p>The following table shows the pooled baseline CIN3+ risk associated with HPV positivity for hierarchically ranked types grouped in four groups according to level of carcinogenicity. Results from available analysed data.</p> <table border="1"> <thead> <tr> <th colspan="3"></th> <th>Pooled CIN3+ risk, in % (95% CI)</th> </tr> <tr> <th>Risk of CIN3+</th> <th></th> <th>Look-alike</th> <th>all studies</th> </tr> <tr> <th>HPV group</th> <th>HPV types</th> <th>HPV groups</th> <th></th> </tr> </thead> <tbody> <tr> <td>1a</td> <td>HPV16</td> <td></td> <td>20.5 (11.2-31.7)</td> </tr> <tr> <td>1b</td> <td>HPV18/45</td> <td></td> <td>7.1 (4.2-10.7)</td> </tr> <tr> <td>1c</td> <td>HPV31/33/35/52/53</td> <td>-HPV35</td> <td>7.3 (4.0-11.4)</td> </tr> <tr> <td>1d</td> <td>HPV39/51/56/59</td> <td>+HPV35/66/68</td> <td>1.9 (1.0-3.2)</td> </tr> </tbody> </table> <p>The GDG agreed that risk of CIN3+ (and downstream cervical cancer over time) varies by HPV DNA type.</p>						Pooled CIN3+ risk, in % (95% CI)	Risk of CIN3+		Look-alike	all studies	HPV group	HPV types	HPV groups		1a	HPV16		20.5 (11.2-31.7)	1b	HPV18/45		7.1 (4.2-10.7)	1c	HPV31/33/35/52/53	-HPV35	7.3 (4.0-11.4)	1d	HPV39/51/56/59	+HPV35/66/68	1.9 (1.0-3.2)
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<sup>4</sup> Demarco M, Hyun N, Carter-Pokras O, Raine-Bennett TR, Cheung L, Chen X et al. A study of type-specific HPV natural history and implications for contemporary cervical cancer screening programs. EClinicalMedicine. 2020;22:100293. (<https://doi.org/10.1016/j.eclinm.2020.100293>).

	<p><b>Modelling of the effects of different HPV screening strategies</b>  Three different levels of follow-up were modelled: 90% (very high), 60% (high) and 30% (low).</p> <p>The following figure is based on the results of the modelling. It presents the percent reduction in lifetime number of cancer deaths in five-yearly primary HPV screening strategies when follow-up rates at all steps of the management pathway are 90% (shown in green – baseline assumptions), 60% (blue) or 30% (red). Shaded regions represent variability depending on triage test modelled (cytology, colposcopy or visual inspection with acetic acid [VIA] triage)</p> <p>Note that similar trends occurred with 10-yearly strategies.</p> <p>The GDG agreed that the incidence of cervical cancer and deaths varied by capacity for follow-up and therefore categorized effects into follow-up greater (high follow-up capacity) or less than 60% (low follow-up capacity).</p> <p>For HPV DNA testing with very high follow-up capacity (90%) there was some difference in the reduction of cervical cancer deaths by the type of HPV screening algorithm used (57–64% for five-yearly screening; 46–55% for 10-yearly screening and 37–44% for twice in lifetime). In settings with high follow-up (60% or more) and low follow-up (less than 60%) capacity the differences are larger (26–58%, 17–47%, 13–37% for high follow-up and 6–53%, 3–41%, 3–32% for low follow-up respectively), with greater reductions when more women were treated based on all or most HPV types (or more details see Figs. 1 and 2 in Web Annex A).</p>
<p><b>Undesirable effects</b></p>	
<p>How substantial are the undesirable anticipated effects?</p>	
<p><b>Judgement</b></p> <ul style="list-style-type: none"> <li><input type="radio"/> Large</li> <li><input type="radio"/> Moderate</li> <li><input type="radio"/> Small</li> <li><input type="radio"/> Trivial</li> <li><input checked="" type="radio"/> <b>Varies</b></li> <li><input type="radio"/> Don't know</li> </ul>	<p><b>Research evidence</b></p> <p>With regards to pre-cancer treatment, the modelling evidence suggests that there are more pre-cancer treatments when treating all women who tested positive for any HPV (not triaging) than when using extended or limited genotyping (at five-yearly intervals, and similarly with 10-yearly). The lowest numbers of pre-cancer treatments occurred when women positive for group 1a or 1b were treated and those positive for group 1c were triaged (and treated if positive on triage), and those positive for group 1d were not treated or when women positive for group 1a or 1b were treated and those positive for other carcinogenic HPV (cHPV) types were triaged (and treated if positive on triage) or when all women who tested positive were triaged with colposcopy.</p>

Primary test	Screening ages	Cervical cancer cases (% reduction)	Cervical cancer deaths (% reduction)	Pre-cancer treatments	NNT to avert a cervical cancer death
No Screening	-	1,950 (-)	1,456 (-)	None	None
12-type (1a-d) treat ('Screen-and-treat')	5yrly, 30-50 yrs (5X)	852 (56%)	525 (64%)	49,967	54
8-type (1a-c) treat ('Screen-and-treat')	5yrly, 30-50 yrs (5X)	936 (52%)	600 (59%)	31,583	37
12-type (1a-d) triage with VIA	5yrly, 30-50 yrs (5X)	938 (52%)	578 (60%)	30,194	34
12-type (1a-d) triage with cytology	5yrly, 30-50 yrs (5X)	1017 (48%)	622 (57%)	20,532	25
12-type (1a-d) triage with colposcopy	5yrly, 30-50 yrs (5X)	939 (52%)	562 (61%)	33,170	37
12-type LG (1a-b) treat, (1c-d) triage with VIA	5yrly, 30-50 yrs (5X)	874 (55%)	539 (63%)	34,357	37
12-type LG (1a-b) treat, (1c-d) triage with cytology	5yrly, 30-50 yrs (5X)	902 (54%)	554 (62%)	26,495	29
12-type LG (1a-b) treat, (1c-d) triage with colposcopy	5yrly, 30-50 yrs (5X)	869 (55%)	529 (64%)	35,924	39
8-type LG (1a-b) treat, 1c triage with VIA	5yrly, 30-50 yrs (5X)	954 (51%)	612 (58%)	25,282	30
8-type LG (1a-b) treat, 1c triage with cytology	5yrly, 30-50 yrs (5X)	969 (50%)	622 (57%)	21,481	26
8-type LG (1a-b) treat, 1c triage with colposcopy	5yrly, 30-50 yrs (5X)	948 (51%)	604 (59%)	25,342	30
12-type EG (1a-c) treat, 1d triage with VIA	5yrly, 30-50 yrs (5X)	858 (56%)	528 (64%)	40,647	44
12-type EG (1a-c) treat, 1d triage with cytology	5yrly, 30-50 yrs (5X)	870 (55%)	535 (63%)	36,548	40
12-type EG (1a-c) treat, 1d triage with colposcopy	5yrly, 30-50 yrs (5X)	850 (56%)	522 (64%)	41,229	44

Certainty of evidence	
What is the overall certainty of the evidence of effects?	
Judgement	Research evidence
<ul style="list-style-type: none"> <li>○ Very low</li> <li>● Low</li> <li>○ Moderate</li> <li>○ High</li> <li>○ No included studies</li> </ul>	<p>Longitudinal studies following women comparing different screening and treatment strategies with extended genotyping to limited or no genotyping are not available. Two other sources of evidence were used: 1) The benefits and harms comparing the different strategies were instead modelled. There was some indirectness due to the assumptions in the model (and structure), and some imprecision around the estimated effects (e.g. around cervical cancer deaths) – resulting in low certainty evidence; and 2) Evidence across multiple studies measuring the cumulative risk up to 10 years of CIN3+ per each cHPV type.</p>

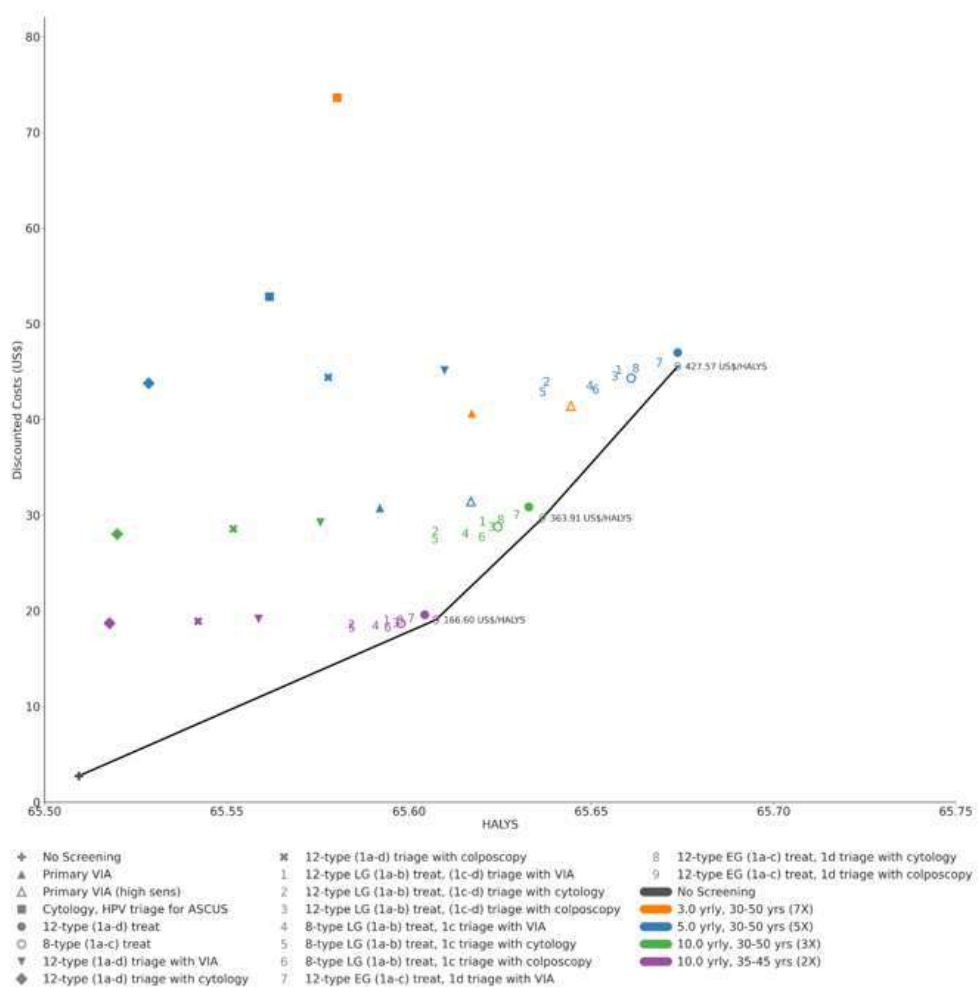
  

Values	
Is there important uncertainty about or variability in how much people value the main outcomes?	
Judgement	Research evidence
<ul style="list-style-type: none"> <li>○ Important uncertainty or variability</li> <li>○ Possibly important uncertainty or variability</li> <li>○ Probably no important uncertainty or variability</li> <li>● No important uncertainty or variability</li> </ul>	<p>The GDG agreed to place the greatest weight on reducing cervical cancer deaths and incidence and less weight on overtreatment. However, the strategy would need to also be cost-effective and consider the capacity of programmes to screen, triage, treat and follow-up and their resources.</p>

Balance of effects																																									
Does the balance between desirable and undesirable effects favour the intervention or the comparison?																																									
Judgement	Research evidence																																								
<ul style="list-style-type: none"> <li>○ Favours the comparison</li> <li>○ Probably favours the comparison</li> <li>○ Does not favour either the intervention or the comparison</li> <li>○ Probably favours the intervention</li> <li>○ Favours the intervention</li> <li>● <b>Varies</b></li> <li>○ Don't know</li> </ul>	<p>In high follow-up settings, the GDG agreed that the use of extended or limited genotyping is probably favoured over no genotyping (there are more benefits [reductions in cervical cancer deaths] than harms [overtreatment]).</p> <p>Treating all HPV-positive women reduces more cancer deaths and is more cost-effective. However, this strategy leads to the larger number of pre-cancer treatments, which in screening programmes with high follow-up capacity can be reduced by using HPV DNA extended or limited genotyping.</p> <p>In low follow-up settings, the GDG agreed that the use of no genotyping (treating all) or limited genotyping is probably favoured over extended genotyping, except when using HPV extended genotyping to treat women positive for any HPV type in groups 1a, 1b or 1c, similarly to using 8 cHPV types tests when those become available.</p>																																								
Resources required																																									
How large are the resource requirements (costs)?																																									
Judgement	Research evidence																																								
<ul style="list-style-type: none"> <li>○ Large costs</li> <li>○ Moderate costs</li> <li>● <b>Negligible costs and savings</b></li> <li>○ Moderate savings</li> <li>○ Large savings</li> <li>○ Varies</li> <li>○ Don't know</li> </ul>	<p>Costs that were considered in the modelling:</p> <p style="text-align: center;"><b>Summary of aggregate costs (average across all 78 LMIC+)</b></p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="background-color: #0056b3; color: white;">Event</th> <th style="background-color: #0056b3; color: white;">Cost (US\$ 2019)</th> <th style="background-color: #0056b3; color: white;">Event</th> <th style="background-color: #0056b3; color: white;">Cost (US\$ 2019)</th> </tr> </thead> <tbody> <tr> <td>Primary VIA<sup>^</sup></td> <td>7.13</td> <td>Histology<sup>®</sup></td> <td>18.14</td> </tr> <tr> <td>Primary HPV (+/- 16/18)<sup>*</sup></td> <td>15.20</td> <td>Punch biopsy/Biopsy</td> <td>11.67</td> </tr> <tr> <td>Primary cytology<sup>^</sup></td> <td>18.13</td> <td>Cancer diagnosis and treatment– FIGO 1<sup>®</sup></td> <td>263.23</td> </tr> <tr> <td>VIA triage<sup>○</sup></td> <td>3.03</td> <td>Cancer diagnosis and treatment– FIGO 2<sup>®</sup></td> <td>546.28</td> </tr> <tr> <td>Cytology triage<sup>○</sup></td> <td>15.74</td> <td>Cancer diagnosis and treatment– FIGO 3<sup>®</sup></td> <td>683.08</td> </tr> <tr> <td>HPV triage<sup>○</sup></td> <td>8.15</td> <td>Cancer diagnosis and treatment– FIGO 4<sup>®</sup></td> <td>312.77</td> </tr> <tr> <td>Colposcopy<sup>○, #</sup></td> <td>9.98</td> <td>Palliative care<sup>®</sup></td> <td>116.92</td> </tr> <tr> <td>Ablative treatment</td> <td>11.77</td> <td>Yearly surveillance after treatment<sup>®</sup></td> <td>58.36</td> </tr> <tr> <td>Excisional treatment</td> <td>41.71</td> <td></td> <td></td> </tr> </tbody> </table> <p><sup>^</sup> Includes workforce, consumables/equipment  <sup>*</sup> Includes cost of test, sample drop-off and transport, laboratory staff time, lab supplies, general administration and overhead costs using WHO-CHOICE methodology and database  <sup>○</sup> Same as primary, but includes a proportion of the labour, programmatic and utilisation costs from primary visits due to not requiring another visit.  <sup>#</sup> Includes consumables/equipment, workforce  <sup>®</sup> Includes consumables/equipment, workforce including pathological and biomedical scientist  <sup>®</sup> Cancer costs are only applied to the proportion of cancers that are treated, and assumed to apply to 90% of screen-detected cases. Yearly surveillance assumed to apply up to 10 years after diagnosis or death, whichever comes first.  <sup>+</sup> The average across 78 LMIC sum the country-level costs weighted by the population of each country, and divides by the total population of those countries combined.</p>	Event	Cost (US\$ 2019)	Event	Cost (US\$ 2019)	Primary VIA <sup>^</sup>	7.13	Histology <sup>®</sup>	18.14	Primary HPV (+/- 16/18) <sup>*</sup>	15.20	Punch biopsy/Biopsy	11.67	Primary cytology <sup>^</sup>	18.13	Cancer diagnosis and treatment– FIGO 1 <sup>®</sup>	263.23	VIA triage <sup>○</sup>	3.03	Cancer diagnosis and treatment– FIGO 2 <sup>®</sup>	546.28	Cytology triage <sup>○</sup>	15.74	Cancer diagnosis and treatment– FIGO 3 <sup>®</sup>	683.08	HPV triage <sup>○</sup>	8.15	Cancer diagnosis and treatment– FIGO 4 <sup>®</sup>	312.77	Colposcopy <sup>○, #</sup>	9.98	Palliative care <sup>®</sup>	116.92	Ablative treatment	11.77	Yearly surveillance after treatment <sup>®</sup>	58.36	Excisional treatment	41.71		
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<b>Cost effectiveness</b> Does the cost-effectiveness of the intervention favour the intervention or the comparison?	
Judgement	Research evidence
<ul style="list-style-type: none"> <li>○ Favours the comparison</li> <li>○ Probably favours the comparison</li> <li>○ Does not favour either the intervention or the comparison</li> <li>○ Probably favours the intervention</li> <li>○ Favours the intervention</li> <li>● <b>Varies</b></li> <li>○ No included studies</li> </ul>	<p>The following graph shows cost-effectiveness for follow-up at 60% (results are similar and all closer to the frontier at 90% of follow-up, not shown).</p> <p>The GDG agreed that strategies that were most cost effective included extended genotyping where most women were treated (groups 1a, b and c) and women in group 1d were triaged.</p>

The following graph shows cost-effectiveness for follow-up less than 60%.



The GDG agreed that strategies that were most cost-effective included strategies where all women who are HPV DNA positive were treated (with no genotyping or limited genotyping).

### Equity

What would be the impact on health equity?

Judgement	Research evidence
<ul style="list-style-type: none"> <li>○ Reduced</li> <li>○ Probably reduced</li> <li>○ Probably no impact</li> <li>○ Probably increased</li> <li>○ Increased</li> <li>● <b>Varies</b></li> <li>○ Don't know</li> </ul>	<p>No research evidence was found. However, the GDG agreed that providing HPV DNA testing may lead to greater access to screening, but extended genotyping may be limited in some settings.</p>

Acceptability	
Is the intervention acceptable to key stakeholders?	
Judgement	Research evidence
<ul style="list-style-type: none"> <li><input type="radio"/> No</li> <li><input type="radio"/> Probably no</li> <li><input checked="" type="radio"/> <b>Probably yes</b></li> <li><input type="radio"/> Yes</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p><b>Systematic review of reviews of provider perspectives conducted for the 2021 guideline<sup>5</sup></b> found a lack of understanding about HPV tests and meaning of positive result; but in low- and middle-income countries, there is the perception that implementing HPV would increase uptake, lead to more treatment (if same day) and be more sensitive to detect precancerous lesions. The GDG agreed that this evidence is still applicable today.</p>
Feasibility	
Is the intervention feasible to implement?	
Judgement	Research evidence
<ul style="list-style-type: none"> <li><input type="radio"/> No</li> <li><input type="radio"/> Probably no</li> <li><input checked="" type="radio"/> <b>Probably yes</b></li> <li><input type="radio"/> Yes</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>The GDG reported some concern about access to HPV extended genotyping tests. There may be confusion about the HPV types and groups, which may affect implementation. The GDG also indicated that programmes may need guidance about how to interpret and assess follow-up and treatment capacity.</p>

<sup>5</sup> WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. Geneva: World Health Organization; 2021 (<https://apps.who.int/iris/handle/10665/342365>).

## Summary of judgements

	Judgement						
Desirable effects	Trivial	Small	Moderate	Large		<b>Varies</b>	Don't know
Undesirable effects	Large	Moderate	Small	Trivial		<b>Varies</b>	Don't know
Certainty of evidence	Very low	<b>Low</b>	Moderate	High			No included studies
Values	Important uncertainty or variability	Possibly important uncertainty or variability	<b>Probably no important uncertainty or variability</b>	No important uncertainty or variability			
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	<b>Varies</b>	Don't know
Resources required	Large costs	Moderate costs	<b>Negligible costs and savings</b>	Moderate savings	Large savings	Varies	Don't know
Cost-effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	<b>Varies</b>	No included studies
Equity	Reduced	Probably reduced	Probably no impact	<b>Probably increased</b>	Increased	Varies	Don't know
Acceptability	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
Feasibility	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know

## Type of recommendation

Strong recommendation against the intervention  ○	<b>Conditional recommendation against the intervention</b>  ●	Conditional recommendation for either the intervention or the comparison  ○	<b>Conditional recommendation for the intervention</b>  ●	Strong recommendation for the intervention  ○
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## Conclusions

### Recommendation for the general population of women

#### Recommendations for settings with high follow-up capacity (60% or greater)

In settings with high follow-up capacity (60% or greater) and sufficient ablative treatment capacity, WHO suggests using HPV DNA testing with extended or limited genotyping OVER treating all HPV-positive women or triaging all HPV-positive women with additional tests.

In settings with high follow-up capacity (60% or greater) and sufficient ablative treatment capacity where HPV DNA extended genotyping is used, WHO suggests:

- treating all eligible women with ablative treatment who test positive for carcinogenic HPV (cHPV) types 16 (group 1a), 18 and 45 (group 1b) and 31, 33, 35, 52 and 58 (group 1c); AND triaging women who test positive for cHPV types 39, 51, 56 and 59 (group 1d);

OVER

- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b) AND triaging women who test positive for cHPV types 31, 33, 35, 52, 58, 39, 51, 56 and 59 (groups 1c and 1d);

OVER

- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b) AND triaging women who test positive for cHPV types 31, 33, 35, 52 and 58 (group 1c) AND returning women who test positive for cHPV types 39, 51, 56 and 59 (group 1d) to routine screening.

*Remark:* To determine the type of treatment, women should be visually evaluated for eligibility for ablative treatment. Women not eligible for ablative treatment should be treated using large-loop excision of the transformation zone (LLETZ) or referred for further management if cancer is suspected.

*Conditional recommendation, low certainty in evidence of effects*

#### Recommendations for settings with low follow-up capacity (less than 60%)

In settings with low follow-up capacity (less than 60%) and sufficient ablative treatment capacity, WHO suggests:

- treating all eligible women with ablative treatment who test positive for any carcinogenic HPV (cHPV) types 16 (group 1a), 18 and 45 (group 1b), 31, 33, 35, 52 and 58 (group 1c), 39, 51, 56 and 59 (group 1d) (consistent with a no-genotyping approach);
- OR treating eligible women with ablative treatment who test positive for any cHPV types 16 (group 1a), 18 and 45 (group 1b) and 31, 33, 35, 52 and 58 (group 1c)<sup>6</sup>

OVER

- treating all eligible women with ablative treatment who test positive for cHPV types 16 (group 1a), 18 and 45 (group 1b) AND triaging women who test positive for cHPV types 31, 33, 35, 52, 58, 39, 51, 56 and 59 (groups 1c and 1d); or

OVER

- triaging with additional tests all women who test positive for any cHPV types (1a, 1b, 1c and 1d)

*Remark:* As the number of visits increases, the risk of loss to follow-up also rises. Although the preferred strategies may result in some overtreatment, they reduce losses to follow-up among women with pre-cancerous lesions who are at high risk of progression to cervical cancer if left untreated.

*Conditional recommendation, low certainty in evidence of effects*

#### Regardless of follow-up capacity

If a programme provides triage with additional tests, WHO suggests using VIA or colposcopic impression (without histological confirmation) as the triage test rather than cytology or dual-stain cytology.

*Remark:* The choice of triage test will depend on availability, installed capacity, feasibility, training and programme quality assurance in countries. To determine treatment type, women should first undergo visual evaluation for eligibility for ablative treatment. Women who are not eligible for ablative treatment should be treated using large-loop excision of the transformation zone (LLETZ) or referred for further management if cancer is suspected.

*Conditional recommendation, low certainty in evidence of effects*

<sup>6</sup> This can be done when using an 8-cHPV type test (tests designed to detect the eight most cHPV types) as per WHO target product profiles for HPV screening tests, or when using extended genotyping HPV tests.

## Justification

Overall, the certainty of the evidence for these recommendations is low and based on modelled outcomes, as data from longitudinal studies providing screening with extended genotyping and following outcomes of individuals is not yet available. The benefits, harms and cost-effectiveness of the strategies using extended, limited or no genotyping varies based on the follow-up capacity and treatment capacity in countries and regions. Although capacity is on a continuum in practice, the model is based on 90%, 60% and 30% capacity. The Guidelines Development Group (GDG) identified that the effects at 60% and 30% capacity were similar and that capacity above 60% may be challenging for many programmes. Therefore a distinction was made between recommendations for settings with 60% and greater follow-up capacity versus less than 60% follow-up capacity. For each of these follow-up capacities, the GDG balanced the reduction in cervical cancer deaths and cervical cancer cases, with the number of treatments (and overtreatment), and with cost-effectiveness to make the recommendations.

In settings with high follow-up capacity, extended genotyping, limited genotyping and no genotyping similarly reduced cervical cancer deaths (benefits) but extended and limited genotyping reduced overtreatment more than no genotyping, whether women were treated immediately or triaged. In settings with low follow-up capacity, extended genotyping resulted in a smaller reduction in cervical cancer deaths due to the need for more follow-up visits. Although no genotyping and limited genotyping resulted in more overtreatment, these strategies led to fewer cervical cancer deaths and were more cost effective.

The GDG agreed that most strategies are probably acceptable and feasible, but it is necessary for programmes to assess their follow-up and treatment capacity. There were no concerns with the potential to create inequities with any strategies.

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